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10/516,705	12/02/2004	Takahito Hara	3056 US0P	1003

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EXAMINER	
BRISTOL, LYNN ANNE	
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1643	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/516,705	HARA ET AL.	
	Examiner	Art Unit	
	LYNN BRISTOL	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/19/08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-64 and 71-77* is/are pending in the application.

4a) Of the above claim(s) *1-11 and 13-64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12 and 71-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/15/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/19/08 has been entered.

2. Claims 1-64 and 71-77 are all the pending claims in the application.

3. Claim 12 was amended and new Claim 77 was added in the Response of12/19/08.

4. The amendment filed on 12/19/08 is considered non-compliant because it fails to meet the requirements of 37 CFR § 1.121, as amended on June 30, 2003 (see *68 Fed. Reg. 38611*, Jun. 30, 2003). However, in order to advance prosecution, rather than mailing a Notice of Non-Compliant Amendment, Applicant is advised of the following errors. Applicants filed a response with amended Claims 72, 73, 74, 75, and 76 on 3/25/08. Applicants will carefully note that the Response including the amended claims were ***not*** entered in the Advisory Action of 4/22/08. Nevertheless, Applicants have now filed a claim set on 12/19/08 having seemingly assumed the amendments from 3/25/08 were entered. The instant claim set for Claims 72, 73, 74, 75, and 76 does not indicate what should be a proper status identifier (i.e., currently amended) and the mark-up of the amended claims.

5. Claims 1-11 and 13-64 are withdrawn from examination.

6. Claims 12 and 71-77 are all the pending claims under examination for this application.

7. Applicants amendments to the claims have necessitated new grounds for rejection.

Information Disclosure Statement

8. The reference cited in the IDS of 1/15/09 has been considered and entered. The initialed and signed 1449 form is attached.

Withdrawal of Objections

Claim Objections

9. The objection to Claims 72 and 76 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn in view of the amendment to change the dependency of Claim 72 to Claim 12 and the dependency of Claim 76 to Claim 73.

Withdrawal of Rejections

Claim Rejections - 35 USC § 112, second paragraph

10. The rejection of Claim 73 in lacking antecedent basis for the limitation "said cancer cells" in line 5 is withdrawn. Claim 73 was amended to recite "culturing cancer cells" in line 3.

11. The rejection of Claim 75 in depending from Claim 72 and not being further limiting but reciting a broadening limitation is withdrawn. Claim 75 was amended to depend from Claim 73.

Claim Rejections - 35 USC § 112, first paragraph

Written Description/New Matter

12. The rejection of Claims 12, 71, 72 and 74-76 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement because the claims recite culturing cells of an androgen-sensitive cancer in the presence of the test substance for "*at least three months*" is withdrawn.

Claim 12 (and dependent Claims 71 and 72) have been amended to recite "at least six weeks", new Claim 77 recites "at least 13 weeks", and Claims 74-76 have been amended to depend from Claim 73 which was not originally rejected. Support for the recited ranges is found on p. 78 at line 9 of the specification.

Biological Deposit

13. The rejection of Claims 73-76 under 35 U.S.C. § 112, first paragraph, for a cancer cell line which comprises a leucine or cysteine substitution for tryptophan at amino acid number 746 of SEQ ID NO:2 (human androgen receptor) which is not known and publicly available, is withdrawn.

Upon further consideration, it is apparent that the ordinary artisan could clone a sequence comprising "a leucine or cysteine substitution for tryptophan at amino acid

number 746 of SEQ ID NO:2" (Claim 73) or a sequence comprising "an alanine substitution for threonine at amino acid number 882 of SEQ ID NO:2" (Claim 74) into an expression vector and transfect any cancer cell or a prostate cancer cell in order to obtain a cancer cell comprising the sequence(s), e.g., mutated androgen receptor.

New Grounds for Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claim 77 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claim 77 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the method step that occurs or is performed for at least 13 weeks on the cells and the test compound.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

15. Claims 73-76 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antiandgrogen drug screening method culturing the test compound in the presence of cancer cells comprising a leucine or cysteine substitution for tryptophan at amino acid number 746 of SEQ ID NO:2 (mutant AR) or an alanine substitution for threonine at amino acid number 882 of SEQ ID NO:2 (mutant AR) for 6 weeks or more, 13 weeks or more or for 6 to 13 weeks, does not reasonably provide enablement for culturing the cells and test compound for an indefinite of undefined amount of time in order to identify a test compound that does not induce antiandrogen drug resistant cell population. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability of the art, the breadth of the claims, the quantity of experimentation which would be required in order to use the invention as claimed.

Nature of the Invention/ Skill in the Art

The claims are interpreted as being drawn to a method for identifying antiandrogen drugs that would prevent proliferation of any cancer cell comprising mutations in the androgen receptor where the cancer cell comprises a leucine or

cysteine substitution for tryptophan at amino acid number 746 of SEQ ID NO:2 (Claim 73) or a sequence comprising "an alanine substitution for threonine at amino acid number 882 of SEQ ID NO:2" (Claim 74), and the cancer cells are human (Claim 75) and the human cancer cells are prostate cancer cells (Claim 76).

Essentially, the mutations in the AR of Claim 73 are induced by bicalutamide as taught by Applicants in Example 1, and the mutations in AR of Claim 74 are induced by flutamide, and therefore at least with respect to the starting population of cancer cells in the assay method, they are bicalutamide-resistant or refractory to bicalutamide and/or flutaminde resistant or refractory to flutaminde.

The relative skill in the art is a drug discovery technologist with a background in screening anti-hormone response drug therapy for cancer.

Disclosure in the Specification

The specification discloses that bicalutamide-resistant cancer cell lines comprising a leucine substitution for tryptophan at amino acid number 746 of SEQ ID NO:2 (LNCaP-cxD 11) or a sequence comprising an or cysteine substitution for tryptophan at amino acid number 746 of SEQ ID NO:2 (LNCaP-cxD2) were generated under long-term culture conditions in Example 1, namely, for 6 weeks or 13 weeks or more.

Prior Art Status: antiandrogen drug resistance occurs after long-term exposure to an antiandrogen and the mutations are drug-dependent

Some clinical findings have been reported concerning the relationship between cancer relapse after antiandrogen drug administration and AR (androgen receptor)

mutations. AR mutations were observed in 5 of 17 patients who experienced relapsed prostate cancer after an endocrine therapy with a combination of flutamide and castration, all of which mutations were missense mutations of the 877th amino acid (corresponding to amino acid number 882 in the amino acid sequence of SEQ ID NO: 2) (Taplin et al., Cancer Res., 59:2511-2515, 1999); cited in the IDS of 12/2/04). On this type of mutant ARs, some antiandrogen drugs, including flutamide, conversely exhibited an action to stimulate cancer cell proliferation (Veldscholte et al., Biochem. Biophys. Res. Commun., 173: 534-540, 1990); cited in the IDS of 12/2/04). Also, although missense mutations of AR were identified in 3 of 11 biopsy samples from patients who experienced relapsed prostate cancer after an endocrine therapy with a combination of bicalutamide and surgical castration, all mutation sites were other than the 877th amino acid, which is a prevalent mutation site in flutamide-resistant relapsed cancers (Haapala et al., Lab. Invest., 81: 1647-1651, 2001); cited in the IDS of 12/2/04). Here Haapala states "Our data does not confirm the accumulation of AR mutations at the codon 877 reported by Taplin et al (1999), which is most likely due to the different anti- androgen used (bicalutamide versus flutamide) in the present study. This observation indicates that different types of AR variants are developed and selected for during bicalutamide and flutamide treatments and supports the data by Han et al (J. Biol. Chem 276:11204-11213 (2001)), who suggested that changes in the hormonal environment may drive the selection of spontaneous somatic mutations that provide a growth advantage for prostate cancer (CaP)." Notable amongst all of these studies is the time lapse for the treatment period in therapy response, so Taplin teaches 20 months; and Haapala

teaches at least 11 months of treatment (see Table 1). Culig et al. (Br. J. Can. 81:242-251 (1999); cited in the PTO 892 form of 1/12/07) teaches that bicalutamide –resistant cancer growth starts to appear in vivo in xenografted prostate cancer cells in mice at around 35 days (or 5 weeks) with bicalutamide treatment (see Figure 7).

Undue Experimentation and Unpredictability

The instant claims are not limited to the culture period for observing whether development of drug-resistant cancer cells would occur under the culture conditions of the method. Thus depending on the antiandrogren drug being tested much less the cell line standarized for the assay method, the ordinary artisan would not have been enabled to practice the method of the instant scope on cancer cell expressing the androgen mutations as claimed much less under culture conditions for an indeterminate and unclaimed amount of time in order to select a drug candidate that does not result in the proliferation of the cancer cell line.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

16. Claims 12, 71, 72 and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Long et al (Can. Res. 60:6630-6640 (2000); cited in the PTO 892 form of 5/15/07) in view of Culig et al. ((Br. J. Can. 81:242-251 (1999); cited in the PTO 892 form of 1/12/07) and Haapala et al., Lab. Invest., 81: 1647-1651, 2001); cited in the IDS of 12/2/04).

Claims 12, 71, 72 and 77 are drawn to a method of screening for antiandrogen drugs which produce little or no cancer resistance, where the method involves culturing an androgen-sensitive cancer cell in the presence of the drug for at least six weeks and determining whether or not the cancer cells proliferate in the presence of the drug (Claim 12), where the cancer cells are human (Claim 71) and the human cancer cells are prostate cancer cells (Claim 72) and where the culture period is at least 13 weeks (Claim 77).

The claimed method was prima facie obvious at the time of the invention over Long, Culig and Haapala.

Long discloses screening antiandrogen compounds for their in vitro growth inhibitory effects on the androgen-dependent prostate cancer cell line, LNCaP. Long discloses using the cell line in culture to compare the efficacy of test compounds $C_{17,20}$-lyase, 5α-reductase, ketoconazole and finasteride with known inhibitor, flutamide, and measuring growth effects in vitro by culturing for 9 days (Figure 2A, Figure 3). Long

observes differences over time in the appearance of the cell line ability to proliferate depending on the culture conditions. Long does not teach culturing for at least 6 weeks or at least 13 weeks whereas does Culig and Haapala.

Culig teaches anti-androgen withdrawal phenomenon may be in part attributed to mutant ARs detected in prostatic carcinomas. Culig teaches that bicalutamide –resistant cancer growth starts to appear in vivo in xenografted prostate cancer cells in mice at around 40 days (or 5.7 weeks) (see Figure 6 and 7) and experiments extending to 65 days (9 weeks) (see Figure 6). Thus Culig at least suggests that bicalutamide – resistance in prostate cancer cells is observable at at least 6 weeks.

Haapala teaches the observation of AR mutations occurring at at least 11 months (at least 6 weeks or at least 13 weeks) of bicalutamide treatment (see Table 1).

One skilled in the art would have been motivated to have produced the drug screening method and been reasonably assured of success at the time the invention was made based on the combined disclosure of Long, Culig and Haapala. The concept of selecting drugs that do not induce androgen resistant cancer cell lines (with or without mutated ARs) over long-term exposure was well understood within the field of art at the time of the invention based on the disclosures of Long, Culig and Haapala. Modifying the assay methods of Long to include incubating the prostate cancer cells in the presence of the test drug for at least 6 or 13 weeks in order to ensure that the cancer cells do not proliferate, or that a population of cells do not become drug resistant or tolerant, would have been obvious to the ordinary artisan in considering the long-terms effects observed for art-known antiandrogen drugs where such resistance had

been observed in vivo. Thus the motivation would have been to develop an assay method that considered screening for drug resistance developing at at least 6 weeks or at at least 13 weeks of drug exposure for any new candidate because of the art-recognized phenomenon for this class of drugs. The ordinary artisan would have been reasonable assured of success in having produced the claimed assay method because the material reagent were available, the establishment of drug screening assay for AR was already established and to change the culture period to ensure that a drug-resistant population of cancer cells did not develop or escaped detection by short term culturing, the artisan would have been motivated to culture for longer periods, i.e., at least 6 weeks or at least 13 weeks.

17. Claims 12, 71, 72 and 77 are rejected under 35 U.S.C. 102(b) as being anticipated by Foury et al (J. Steroid Biochem. Molec. Biol. 66:235-240 (1998); cited in the PTO 892 form of 5/15/07) in view of Culig et al. ((Br. J. Can. 81:242-251 (1999); cited in the PTO 892 form of 1/12/07) and Haapala et al., Lab. Invest., 81: 1647-1651, 2001); cited in the IDS of 12/2/04).

The interpretation of Claims 12, 71, 72 and 77 is discussed above under section 16.

The claimed method was prima facie obvious at the time of the invention over Foury, Culig and Haapala.

Foury discloses comparing androgen responsive cell lines (LNCaP, R2 and MOP) *in vitro* for ability to proliferate in studies comparing two different antiandrogen

drugs (CYPA and RU 56187). Foury discloses that R2 is inhibited by RU 56187 and MOP is inhibited by CYPA and RU 56187. Foury observes differences over time in the appearance of the different cell lines abilities to proliferate depending on the culture conditions. Foury does not teach culturing for at least 6 weeks or at least 13 weeks whereas does Culig and Haapala.

Culig teaches anti-androgen withdrawal phenomenon may be in part attributed to mutant ARs detected in prostatic carcinomas. Culig teaches that bicalutamide –resistant cancer growth starts to appear in vivo in xenografted prostate cancer cells in mice at around 40 days (or 5.7 weeks) (see Figure 6 and 7) and experiments extending to 65 days (9 weeks) (see Figure 6). Thus Culig at least suggests that bicalutamide – resistance in prostate cancer cells is observable at at least 6 weeks.

Haapala teaches the observation of AR mutations occurring at at least 11 months (at least 6 weeks or at least 13 weeks) of bicalutamide treatment (see Table 1).

One skilled in the art would have been motivated to have produced the drug screening method and been reasonably assured of success at the time the invention was made based on the combined disclosure of Foury, Culig and Haapala. The concept of selecting drugs that do not induce androgen resistant cancer cell lines (with or without mutated ARs) over long-term exposure was well understood within the field of art at the time of the invention based on the disclosures of Foury, Culig and Haapala. Modifying the assay methods of Foury to include incubating the prostate cancer cells in the presence of the test drug for at least 6 or 13 weeks in order to ensure that the cancer cells do not proliferate, or that a population of cells do not become drug resistant

or tolerant, would have been obvious to the ordinary artisan in considering the long-terms effects observed for art-known antiandrogen drugs where such resistance had been observed in vivo. Thus the motivation would have been to develop an assay method that considered screening for drug resistance developing at at least 6 weeks or at at least 13 weeks of drug exposure for any new candidate because of the art-recognized phenomenon for this class of drugs. The ordinary artisan would have been reasonably assured of success in having produced the claimed assay method because the material reagent were available, the establishment of drug screening assay for AR was already established and to change the culture period to ensure that a drug-resistant population of cancer cells did not develop or escaped detection by short term culturing, the artisan would have been motivated to culture for longer periods, i.e., at least 6 weeks or at least 13 weeks.

18. Claims 12, 71, 72 and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Taplin et al. (Cancer Research, (1999), pp. 2511-2515, Vol. 59, No. 11; cited in the IDS of 12/2/04) in view of Joly-Pharaboz et al (J. Steroid Biochem. Molec. Biol. 55:67-76 (1995); cited in the PTO 892 form of 5/15/07) and further in view of Culig et al. ((Br. J. Can. 81:242-251 (1999); cited in the PTO 892 form of 1/12/07) and Haapala et al., Lab. Invest., 81: 1647-1651, 2001); cited in the IDS of 12/2/04).

The interpretation of Claims 12, 71, 72 and 77 is discussed above under section 16.

At the time of Applicants invention, it would have been obvious to have used an *in vitro* antiandrogen drug selection process for identifying drugs that do not induce cancer resistance using a cancer cell line based on the combined disclosures of Taplin, Joly-Pharaboz, Culig and Haapala.

Taplin discloses that AR mutations in tumor cells occur in response to strong selective pressure from flutamide (antiandrogen) treatment *in vivo* and that these mutations result in drug resistance for some patients and continued tumor cell survival and proliferation. Taplin discloses that other methods are needed to prevent a small number of tumor cells from surviving or escaping the initial inhibitory effects of AR antagonists such as targeting AR-associated coactivator proteins, downstream target genes, or signal transduction pathways that interact with AR which can be used alone or in combination with androgen blockade therapy. Taplin does not disclose an in vitro drug screening method which Joly-Pharaboz recitifies in its disclosure.

Joly-Pharaboz disclose drug selection for androgen-responsive cell lines *in vitro* under culture conditions with chronic treatment of androgens and antiandrogens, where cell proliferation under long-term culture is used to assess induction of drug resistance. Joly-Pharaboz discloses the antiandrogen drugs, hydroxyflutaminde or cyproteropne acetate, as examples of drugs that induce cell proliferation in the screening method. Joly-Pharaboz does not teach culturing for at least 6 weeks or at least 13 weeks whereas does Culig and Haapala.

Culig teaches anti-androgen withdrawal phenomenon may be in part attributed to mutant ARs detected in prostatic carcinomas. Culig teaches that bicalutamide –resistant

cancer growth starts to appear in vivo in xenografted prostate cancer cells in mice at around 40 days (or 5.7 weeks) (see Figure 6 and 7) and experiments extending to 65 days (9 weeks) (see Figure 6). Thus Culig at least suggests that bicalutamide – resistance in prostate cancer cells is observable at at least 6 weeks.

Haapala teaches the observation of AR mutations occurring at at least 11 months (at least 6 weeks or at least 13 weeks) of bicalutamide treatment (see Table 1).

One skilled in the art would have been motivated to have produced the drug screening method and been reasonably assured of success at the invention was made based on the combined disclosure of Taplin, Joly-Pharaboz, Culig and Haapala. The concept of selecting drugs that do not induce resistant cancer cell lines (with or without mutated ARs) was well understood within the field of art at the time of the invention. Taplin teaches induction of antiandrogen resistant cancer cells *in vivo* and the need to identify other methods that target tumor cells that escape the effects of antiandrogen drugs such as observed with flutamide, and Joly-Pharaboz disclose successful *in vitro* drug selection methods using drug-cultured cells from androgen-sensitive cancers where sensitivity to the drug is measured by inhibition of cell proliferation. Modifying the assay methods of Joly-Pharaboz to include incubating the prostate cancer cells in the presence of the test drug for at least 6 or 13 weeks in order to ensure that the cancer cells do not proliferate, or that a population of cells do not become drug resistant or tolerant, would have been obvious to the ordinary artisan in considering the long-terms effects observed for art-known antiandrogen drugs where such resistance had been observed in vivo. Thus the motivation would have been to develop an assay method

that considered screening for drug resistance developing at at least 6 weeks or at at least 13 weeks of drug exposure for any new candidate because of the art-recognized phenomenon for this class of drugs.

One skilled in the art would have been assured of success in creating the instant claimed method because Taplin discloses the problems with administering a single antiandrogen drug over long-term treatment and the need to identify other inhibitors associated with AR or tumor targeting and Joly-Pharaboz already appreciated in vitro drug screening to select for antiandrogens that do not induce cancer resistance. The ordinary artisan would have been reasonably assured of success in having produced the claimed assay method because the material reagent were available, the establishment of drug screening assay for AR was already established and to change the culture period to ensure that a drug-resistant population of cancer cells did not develop or escaped detection by short term culturing, the artisan would have been motivated to culture for longer periods, i.e., at least 6 weeks or at least 13 weeks.

For all of these reasons, the claimed invention was prima facie obvious over Taplin, Joly-Pharaboz, Culig and Haapala.

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Conclusion

19. No claims are allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lynn A. Bristol/
Examiner, Art Unit 1643
Partial Signatory Authority